REMARKS

Status of the claims

Claim 3 is amended. Claims 2 and 4-20 are canceled. Claims 1, 3 and 18 are pending in the application. Claims 1, 3 and 18 are rejected.

Claim Amendments

Claim 3 is amended to add the correct identifier "(currently amended)" to overcome the objection to this claim. Claim 18 is canceled herein to overcome the objection that it is a substantial duplicate of claim 3. No new matter is added.

Claim Objections

Claim 3 is objected to because of the incorrect identifier "(original)". Claim 3 has been amended to replace the incorrect identifier with the correct identifier "(currently amended)".

Claim 18 is objected to because it is a substantial duplicate of claim 3. Claim 18 is herein canceled to overcome this objection.

Claim rejection under 35 U.S.C. § 112

Claim 1 is rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the enablement requirement. The Applicant respectfully traverses this rejection.

The examiner states that the specification does not provide enablement of the claim as presented but provides enablement for making an Elux mouse, having cells comprising the firefly luciferase transgene operably linked to an E2F1 promoter. The Examiner contends that specific guidance to use a particular luciferase does not necessarily predict guidance to use another luciferase (pg. 4, lines 8-9). The Applicant respectfully disagrees. The Applicant submits that luciferase genes from different sources and their respective substrates are well documented in literature because of their extensive use as reporter genes and also because of their use in bioluminescent assays. Thus it would be relatively easy for one skilled in the art to substitute the firefly luciferase used in the instant invention with another luciferase using the guidelines as laid down in the instant specification. Also, many of the luciferase genes and their substrates are available for example from Xenogen and Promega which can be procured and substituted for the firefly luciferase used in the instant invention. The E2F1 promoter is specified in the instant disclosure and one skilled in the art has to only operably link a luciferase gene to this promoter to use the invention with a different luciferase. Such techniques are well established in the field of molecular and cell biology and are routine laboratory procedures. Accordingly, the Applicant submits that one skilled in the art can easily substitute the firefly luciferase with any other luciferase using the guidance provided in the specification of the present invention.

The Examiner further states that the kinetics of light production and the peak wavelengths for light produced by different luciferases is not the same. According to the Examiner, a skilled practitioner would not be able to predict how to practice the claimed invention with different luciferases. The Applicant respectfully disagrees.

The Applicant submits that the use of higly sensitive CCD cameras is well known in the art of imaging tissues and organs. Bhaumik and Ghambir (PNAS 99(1): 377-382, 2002), as pointed out by the Examiner, have demonstrated that a CCD camera can be used to detect bioluminescence produced by firefly luciferase (λ_{max} = 575 nm, Steghens et al. (1998) biochem. J. 336:109-113; pg. 110, Fig. 1) and Renilla luciferase (λ_{max} = 480 nm, markova et al. 92004) j. Biol. Chem. 279: 3212-3217; pg. 3214, Fig. 1). This clearly indicates that highly sensitive optical devices that can detect light of λ_{max} < 600 are standard in the art. The detection of light of different wavelength essentially depends on the choice of optical filters used in the camera. Furthermore Bhaumik and Ghambir state that although most of the bioluminescent light is likely to be scattered and absorbed, enough escapes from the animal to be detected by a highly sensitive cooled CCD camera (pg. 382, third paragraph). Accordingly, the Applicant submits that In view of what is known in the art it is routine for a person having ordinary skill in this art to use a CCD camera with the correct combination of filters and sensitivity to image light produced by

luciferases that emit light of wavelengths different from firefly luciferase and practice the instant invention.

The Examiner further contends that the full embodiment of the claimed invention encompasses reporter genes coding for non luciferase proteins. The Applicant respectfully disagrees. The Applicant submits that the claims were amended in the previous response filed on March 18, 2005, to recite only to luciferase proteins and exclude all other proteins. Accordingly claim 1 is well within the scope of the instant specification.

The Examiner further contends that "specific guidance to use a reporter gene that encodes firefly luciferase does not necessarily predict guidance to use a reporter gene that encodes any protein capable of producing light upon metabolizing a substrate because there are no known common structures or coding sequences that distinguish said proteins" (pg. 4 lines 14-18). Applicant respectfully disagrees.

Applicant submits that the specification provides sufficient guidelines to prepare a plasmid DNA with an E2F1 promoter and firefly luciferase reporter gene. To prepare such a construct with another luciferase one does not require sequence or structural homology between the firefly luciferase and the other luciferase. The functional aspect of the protein to produce light in the presence of a suitable substrate is what is important and the structural aspects of

the luciferase are not relevant for the instant application. Thus the guidelines presented in the instant invention can be easily extrapolated by techniques well known to a person having ordinary skill in this art to prepare a plasmid DNA with an E2F1 promoter and a luciferase gene other than the firefly luciferase gene. Accordingly the applicant submits that the firefly luciferase can be substituted with any other luciferase as the reporter gene in the instant application.

The Examiner further states that the technology for making transgenic mice is unpredictable and so the "successful construction of a transgenic mouse expressing a firefly luciferase protein is not predictive of success for construction of mice expressing any other luciferase proteins" (pg. 6, lines 5-7). The Applicant respectfully disagrees.

The Applicant submits that the technology of making transgenic mice is not unpredictable. The first transgenic mice were made way back in 1982 by Palmiter and Brinster and since then the technology has advanced rapidly. The elucidation of the mouse genome and recent developments in molecular and cell biology have helped overcome many of the problems associated with making transgenic mice. The method of making transgenic mice is also documented in a number of laboratory handbooks and manuals some of which were published even before 1990. There are also a number of core facilities that can make a transgenic mouse if the transgene is submitted to the core facility. These points definitely indicate that the technology for making transgenic mice is maturity and

is not unpredictable as stated by the Examiner. The Applicant in the instant invention has also successfully demonstrated that an Elux mouse can be prepared using standard techniques known in the art of making transgenic mice. Accordingly in view of the current state of the technology for making transgenic mice, Applicant submits that making a transgenic mouse with any luciferase per the guidelines of the instant specification would be relatively easy for one skilled in the art and would not require undue investigative experimental work. As discussed supra this would only entail operably linking the required luciferase gene to the E2F1 promoter and using this construct to prepare a transgenic mouse as per standard protocols. It is well known in the art of making transgenic mice that for any one transgenic DNA construct a series of transgenic mice are usually obtained, each one likely showing different levels of transgenic gene expression. Therefore, generating a new E2F-luciferase transgenic akin to the one shown in the examples will require as much experimentation as generating a useful transgenic mice having a construct different to the one shown in the examples. This is not considered undue experimentation but a regular part of making a transgene expressing transgenic mice.

In view of what is known and standard in the art, the guidance provided by the instant specification is sufficient for one skilled in the art to make and use the invention, as presented in claim 1. Accordingly, in view of the arguments presented herein, Applicant respectfully requests that the rejection of claim 1 under 35 U.S.C. 112, first paragraph, be withdrawn.

This is intended to be a complete response to the Final Office Action mailed June 20, 2005. Applicant submits that the pending claims 1 and 3 are in condition for allowance and respectfully request that these claims be passed to issuance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution. Please debit any insufficiency in the fees from Deposit Account No. 07-1185 upon which the undersigned is allowed to draw.

Respectfully submitted,

Date: Sept 27, 2005

Benjamin Aaron Adler, Ph.D., J.D.
Registration No. 35,423
Counsel for Applicant

ADLER & ASSOCIATES
8011 Candle Lane
Houston, Texas 77071
(713) 270-5391 (tel.)
(713) 270-5361 (facs.)
badler1@houston.rr.com